

WHAT IS CLAIMED IS:

- 1 *sub 99* 1. An isolated ATP-binding cassette protein having the following
 2 properties:
 3 i. conferring mitoxantrone resistance to a S1-M1-80 human colon
 4 carcinoma cells when expressed in the cells; and,
 5 ii. specifically binding to polyclonal antibodies which specifically
 6 bind to a member of the group of proteins depicted in Seq. ID. No. 2 or ID. No. 4; and
 7 iii. having a molecular weight between about 70 kDa and about 75
 8 kDa.
- 1 2. The ATP-binding cassette protein of claim 1 wherein the protein
 2 has 95% identity to the amino acids depicted in Seq. ID. No. 2 or ID. No. 4.
- 1 3. A eukaryote cell genetically altered to overexpress an ATP-binding
 2 cassette protein having the following properties:
 3 i. conferring mitoxantrone resistance on S1-M1-80 human colon
 4 carcinoma cells when expressed in the cells; and,
 5 ii. specifically binding to polyclonal antibodies which specifically
 6 bind to a member of the group of proteins depicted in Seq. ID. No. 2 or ID. No. 4.
- 1 4. A cell of claim 3, wherein the cell is genetically altered by
 2 transformation of the cell with an exogenous DNA comprising an expression cassette
 3 encoding the ATP-binding cassette protein.
- 1 5. A cell of claim 4, wherein the expression cassette comprises a
 2 heterologous promoter operatively linked to the DNA encoding the ATP-binding cassette
 3 protein.
- 1 6. A cell of claim 3, wherein the cell has an endogenous copy of the
 2 ATP-binding cassette protein and the genetic alteration comprises insertion of DNA
 3 which can serve as an enhancing element or as a second promoter where the insertion is
 4 upstream of the endogenous promoter operatively linked to the ATP-binding cassette
 5 protein and where the inserted DNA increases the basal expression levels of ATP-binding
 6 cassette protein.

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7. A DNA encoding a ATP-binding cassette protein wherein the protein is characterized by having the following properties:

- i. conferring mitoxantrone resistance on S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
- ii. specifically binding to polyclonal antibodies which specifically bind to a member of the group of proteins consisting of those depicted in Seq. ID. No. 2 or ID. No. 4.

8. The DNA of claim 7, wherein the encoded protein has 95% identity to the amino acids depicted in Seq. ID. No. 2 or ID. No. 4.

9. The DNA of claim 7, wherein the DNA encoding the protein has a sequence identical to that depicted in Seq. ID. No. 1 or No. 3.

10. A process for over expressing ATP-binding cassette protein in a cell comprising a first step of either:

- i. transforming the cell with an expression cassette which directs the expression of ATP-binding cassette protein; or,
- ii. selecting a cell having an endogenous copy of the ATP-binding cassette protein, and transforming the cell with DNA which can serve as an enhancing element or as a second promoter where the insertion is upstream of the endogenous promoter operatively linked to the ATP-binding cassette protein and where the inserted DNA increases the basal expression levels of ATP-binding cassette protein; and a second step of,

culturing the transformed cell under conditions where the levels of ATP-binding cassette protein are increased above the basal levels of the non-transformed cells with the proviso that the ATP-binding cassette protein has the following properties:

- a. confers mitoxantrone resistance on S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
- b. specifically binds to polyclonal antibodies which specifically bind to a member of the group of proteins depicted in Seq. ID. No. 2 or ID. No. 4.

1 11. The process of claim 10, wherein the ATP-binding cassette protein
2 has 95% homology to the amino acids depicted in Seq. ID. No. 2 or ID. No. 4.

1 12. The process of claim 10, wherein the protein has the amino acids
2 depicted in Seq. ID. No. 2 or ID. No. 4.

1 13. A method of screening for inhibitors of cytotoxin resistance in cells
2 comprising the steps of:

3 (a) culturing a cell genetically altered by the introduction of
4 heterologous DNA which permits the overexpression an ATP-binding cassette protein
5 where the protein has the following properties:

6 i. conferring mitoxantrone resistance on S1-M1-80 human
7 colon carcinoma cells when expressed in the cells; and,

8 ii. specifically binding to polyclonal antibodies which
9 specifically bind to a member of the group of proteins depicted in Seq. ID. No. 2
10 or ID. No. 4;

11 (b) contacting the cell with a cytotoxin in an amount that permits cell
12 survival due to the resistance conferred by the ATP-binding cassette protein;

13 (c) contacting the cell with a compound that inhibits the biological activity
14 of the ATP-binding cassette protein;

15 (d) detecting the inhibition by measuring growth inhibition of the cells.

1 14. A method of claim 13, where the cytotoxin is mitoxantrone.

1 15. A method of claim 13, where the cytotoxin is daunomycin.

1 16. A method of claim 13, where the cell is a carcinoma cell.

1 *Sub* 17. A method of claim 13, wherein the ATP-binding cassette protein
2 *aid* has 95% homology to the amino acids depicted in Seq. ID. No. 2 or ID. No. 4.

1 18. A binding protein which specifically binds to an ATP-binding
2 cassette protein which has 95% homology to the amino acids depicted in Seq. ID. No. 2
3 or ID. No. 4.

1 19. A binding protein of claim 18, wherein the binding protein is an
2 antibody.

1 20. A binding protein of claim 18, wherein the binding protein is a
2 monoclonal antibody.

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